AMENDMENTS

In the Specification

Added Paragraphs

At page 14, after the first full paragraph, insert the following paragraphs:

--Further, amylin agonist analogues useful in the methods of this application include amylin agonist analogues having the following amino acid sequence:

$^{1}A_1$-X-Asn-Thr-^{5}Ala-Thr-Y-Ala-Thr-^{10}Gln-Arg-Leu-

B_1-Asn-^{15}Phe-Leu-C_1-D_1-E_1-$^{20}F_1$-G_1-Asn-H_1-Gly-$^{25}I_1$-J_1-

Leu-K_1-L_1-^{30}Thr-M_1-Val-Gly-Ser-^{35}Asn-Thr-Tyr-Z

wherein:

A_1 is hydrogen Lys, Ser, Ala, des-α-amino Lys, or acetylated Lys;

B_1 is Ala, Ser or Thr;

C_1 is Val, Leu or Ile;

D_1 is His or Arg;

E_1 is Ser or Thr;

F_1 is Ser, Thr, Gln or Asn;

G_1 is Asn, Gln or His;

H_1 is Phe, Leu or Tyr;

I_1 is Ala or Pro;

J_1 is Ile, Val, Ala or Leu;

K_1 is Ser, Pro, Leu, Ile or Thr;

L_1 is Ser, Pro or Thr;

M_1 is Asn, Asp or Gln;

X and Y are independently selected residues having side chains which are chemically bonded to each other to form an intramolecular linkage; and

Z is hydroxy, amino, alkylamino, dialkylamino, cycloalkylamino, arylamino, aralkylamino, alkyloxy, aryloxy or aralkyloxy;

provided that:

(a) when A_1 is Lys, B_1 is Ala, C_1 is Val, D_1 is His, E_1 is Ser, F_1 is Ser, G_1 is Asn, H_1 is Phe, I_1 is Ala, J_1 is Ile, K_1 is Ser, L_1 is Ser, and M_1 is Asn;

(b) when A_1 is Lys, B_1 is Ala, C_1 is Ile, D_1 is Arg, E_1 is Ser, F_1 is Ser, G_1 is Asn, H_1 is Leu, I_1 is Ala, J_1 is Ile, K_1 is Ser, L_1 is Pro, and M_1 is Asn;

(c) when A_1 is Lys, B_1 is Ala, C_1 is Val, D_1 is Arg, E_1 is Thr, F_1 is Ser, G_1 is Asn, H_1 is Leu, I_1 is Ala, J_1 is Ile, K_1 is Ser, L_1 is Pro, and M_1 is Asn;

(d) when A_1 is Lys, B_1 is Ala, C_1 is Val, D_1 is Arg, E_1 is Ser, F_1 is Ser, G_1 is Asn, H_1 is Leu, I_1 is Pro, J_1 is Val, K_1 is Pro, L_1 is Pro, and M_1 is Asn;

(e) when A_1 is Lys, B_1 is Ala, C_1 is Val, D_1 is His, E_1 is Ser, F_1 is Asn, G_1 is Asn, H_1 is Leu, I_1 is Pro, J_1 is Val, K_1 is Ser, L_1 is Pro and M_1 is Asn; or

(f) when A_1 is Lys, B_1 is Thr, C_1 is Val, D_1 is Arg, E_1 is Ser, F_1 is Ser, G_1 is His, H_1 is Leu, I_1 is Ala, J_1 is Ala, K_1 is Leu, L_1 is Pro and M_1 is Asp;

then one or more of any of A_1 to M_1 is not an L-amino acid and Z is not amino.

Suitable side chains for X and Y include groups derived from alkyl sulfhydryls which may form disulfide bonds; alkyl acids and alkyl amines which may form cyclic lactams; alkyl aldehydes or alkyl halides and alkylamines which may condense and be reduced to form an alkyl amine bridge; or side chains which may be connected to form an alkyl, alkenyl, alkynyl, ether or thioether bond. Preferred alkyl chains include lower alkyl groups having from about 1 to about 6 carbon atoms.

As used herein, the following terms have the following meanings unless expressly stated to the contrary:

The term "alkyl" refers to both straight- and branched-chain alkyl groups. The term "lower alkyl" refers to both straight- and branched-chain alkyl groups having a total of from 1 to 6 carbon atoms and includes primary, secondary, and tertiary alkyl groups. Typical lower alkyls include, for example, methyl, ethyl, n-propyl, isopropyl, n-butyl, isobutyl, t-butyl, n-pentyl, n-hexyl, and the like.

The term "aryl" refers to carbocyclic aromatic groups of 6 to 14 carbon atoms such as phenyl and naphthyl, as well as heterocyclic aromatic groups containing 1 to 3 heteroatoms (nitrogen, oxygen, sulfur, etc.) such as pyridyl, triazolopyrazine, pyrimidine and the like.

The term "aralkyl" refers to an "aryl" group of 6 to 10 carbon atoms directly attached to an "alkyl" group of 1 to 4 carbon atoms and includes for example benzyl, p-chlorobenzyl, p-methylbenzyl, and 2-phenylethyl.

The term "cycloalkyl" refers to cyclic alkyl groups of 5 to 8 carbon atoms.

Biologically active derivatives of the above agonist analogues are also included within the scope of amylin agonist analogues useful in the present invention in which the stereochemistry of individual amino acids may be inverted from (L)/S to (D)/R at one or more specific sites. Also included within the scope of amylin agonist analogues useful in the present invention are the agonist analogues modified by glycosylation of Asn, Ser and/or Thr residues.

Biologically active agonist analogues of amylin which contain less peptide character are also included in the scope of amylin agonist analogues useful in the present invention. Such peptide mimetics may include, for example, one or more of the following substitutions for -CO-NH- amide bonds: depsipeptides (-CO-O-), iminomethylenes ($-CH_2-NH-$), *trans*-alkenes (-CH=CH-), ß-enaminonitriles (-C(=CH-CN)-NH-), thioamides (-CS-NH-), thiomethylenes ($-S-CH_2-$ or $-CH_2-S-$), methylenes, and retro-amides (-NH-CO-).

The above-described amylin agonist analogues form salts with various inorganic and organic acids and bases. Such salts include salts prepared with organic and inorganic acids, for example, HCl, HBr, H_2SO_4, H_3PO_4, trifluoroacetic acid, acetic acid, formic acid, methanesulfonic acid, toluenesulfonic acid, maleic acid, fumaric acid, and camphorsulfonic acid. Salts prepared with bases include, for example, ammonium salts, alkali metal salts (such as sodium and potassium salts), and alkali earth salts (such as calcium and magnesium salts). Acetate, hydrochloride, and trifluoroacetate salts are preferred.

The salts may be formed by conventional means, as by reacting the free acid or base forms of the product with one or more equivalents of the appropriate base or acid in a solvent or medium in which the salt is insoluble, or in a solvent such as water which is then removed in vacuo or by freeze-drying or by exchanging the ions of an existing salt for another

ion on a suitable ion exchange resin. The above-described amylin agonist analogues include various stereoisomers. In the preferred amylin agonist analogues, the chiral centers on the peptide backbone are all S.--

At page 40, after the last paragraph, please insert the following paragraphs:

--To assist in understanding the present invention, the following further Examples A-N are included and describe the results of a series of experiments therein. The following examples relating to this invention should not, of course, be construed as specifically limiting the invention. Such variations of the invention, now known or later developed, which would be within the purview of one skilled in the art are considered to fall within the scope of the present invention as hereinafter claimed.

EXAMPLE A

Preparation of ^{28}Pro-human-Amylin

Solid phase synthesis of this analogue of human ("h-") amylin using methylbenzhydrylamine anchor-bond resin and N^{a}-Boc/benzyl-side chain protection was carried out by standard peptide synthesis methods. The ^{2,7}-[disulfide]amylin-MBHA-resin was obtained by treatment of Acm-protected cysteines with thallium (III) trifluoroacetate in trifluoroacetic acid. After cyclization was achieved, the resin and side chain protecting groups were cleaved with liquid hydrofluoric acid ("HF") in the presence of dimethylsulfide and anisole. The ^{28}Pro-h-amylin was purified by preparative HPLC. The peptide was found to be homogeneous

by analytical HPLC and capillary electrophoresis and the structure was confirmed by amino acid analysis and sequence analysis. The product gave the desired mass ion. FAB mass spec: (M+1)/e=3914.

EXAMPLE B

Preparation of $^{25}Pro^{26}Val^{28,29}Pro$-h-Amylin

Solid phase synthesis of this amylin analogue using methylbenzhydrylamine anchor-bond resin and N^{a}-Boc/benzyl-side chain protection was carried out by standard peptide synthesis methods. The ^{2,7}-[disulfide]amylin-MBHA-resin was obtained by treatment with thallium (III) trifluoroacetate in trifluoroacetic acid. After cyclization was achieved, the resin and side chain protecting groups were cleaved with liquid HF in the presence of dimethylsulfide and anisole. The $^{25}Pro^{26}Val^{28,29}Pro$-h-amylin was purified by preparative HPLC. The peptide was found to be homogeneous by analytical HPLC and capillary electrophoresis and the structure was confirmed by amino acid analysis and sequence analysis. The product gave the desired mass ion. FAB mass spec: (M+1)/e=3936.

EXAMPLE C

Preparation of ^{2,7}Cyclo-[^{2}Asp,^{7}Lys]-h-Amylin

Solid phase synthesis of this amylin analogue using methylbenzhydrylamine anchor-bond resin and N^{a}-Boc/benzyl-side chain protection was carried out by standard peptide synthesis methods. ^{2}Asp and ^{7}Lys were introduced with Boc-^{2}Asp(Fmoc)-OH and Boc-^{7}Lys(Fmoc)-OH. Following selective side-chain deprotection with piperidine, the side-chain to side-chain (^{2}Asp-^{7}Lys) cyclization was carried out using

benzotriazol-1yl-oxy-tris(dimethylamino)-phosphonium hexafluorophosphate (BOP reagent). Cyclization was as described in Di Maio, J., *et al.*, J. Med. Chem., 33:661-667 (1990); and Felix, A.M., *et al.*, Int. J. Pept. Prot. Res., 32:441 (1988). The ^{2,7}cyclo-[^{2}Asp,^{7}Lys]amylin-MBHA-resin obtained after cyclization was cleaved with liquid HF in the presence of dimethylsulfide and anisole. The ^{2,7}cyclo-[^{2}Asp,^{7}Lys]-h-amylin was purified by preparative HPLC. The peptide was found to be homogeneous by analytical HPLC and capillary electrophoresis and the structure was confirmed by amino acid analysis and sequence analysis. FAB mass spec: (M+1)/e=3925.

EXAMPLE D

Preparation of des-^{1}Lys-h-Amylin

Solid phase synthesis of des-^{1}Lys-h-amylin (also represented as $^{2-37}$h-amylin) using methylbenzhydrylamine anchor-bond resin and N^{a}-Boc/benzyl-side chain protection was carried out by standard peptide synthesis methods. The ^{2,7}-[disulfide]amylin-MBHA-resin was obtained by treatment of Acm-protected cysteines with thallium (III) trifluoroacetate in trifluoroacetic acid. After cyclization was achieved, the resin and side chain protecting groups were cleaved with liquid HF in the presence of dimethylsulfide and anisole. The des-^{1}Lys-h-amylin was purified by preparative reversed-phase HPLC. The peptide was found to be homogeneous by analytical HPLC and capillary electrophoresis and the structure was confirmed by amino acid analysis and sequence analysis. The product gave the desired mass ion. FAB mass spec: $(M+H)^{+}$=3,775.

EXAMPLE E

Preparation of ^{1}Ala-h-Amylin

Solid phase synthesis of ^{1}Ala-h-amylin using methylbenzhydrylamine anchor-bond resin and N^{a}-Boc/benzyl-side chain protection was carried out by standard peptide synthesis methods. The ^{2,7}-[disulfide]amylin-MBHA-resin was obtained by treatment of Acm-protected cysteines with thallium (III) trifluoroacetate in trifluoroacetic acid. After cyclization was achieved, the resin and side chain protecting groups were cleaved with liquid HF in the presence of dimethylsulfide and anisole. The ^{1}Ala-h-amylin was purified by preparative reversed-phase HPLC. The peptide was found to be homogeneous by analytical HPLC and capillary electrophoresis and the structure was confirmed by amino acid analysis and sequence analysis. The product gave the desired mass ion. FAB mass spec: $(M+H)^{+}$=3,847.

EXAMPLE F

Preparation of ^{1}Ser-h-Amylin

Solid phase synthesis of ^{1}Ser-h-amylin using methylbenzhydrylamine anchor-bond resin and N^{a}-Boc/benzyl-side chain protection was carried out by standard peptide synthesis methods. The ^{2,7}-[disulfide]amylin-MBHA-resin was obtained by treatment of Acm-protected cysteines with thallium (III) trifluoroacetate in trifluoroacetic acid. After cyclization was achieved, the resin and side chain protecting groups were cleaved with liquid HF in the presence of dimethylsulfide and anisole. The ^{1}Ser-h-amylin was purified by preparative reversed-phase HPLC. The peptide was found to be homogeneous by analytical HPLC and

capillary electrophoresis and the structure was confirmed by amino acid analysis and sequence analysis. The product gave the desired mass ion. FAB mass spec: $(M+H)^+$=3,863.

EXAMPLE G

Preparation of ^{29}Pro-h-Amylin

Solid phase synthesis of this analogue of human amylin using methylbenzhydrylamine anchor-bond resin and N^a-Boc/benzyl-side chain protection was carried out by standard peptide synthesis methods. The ^{2,7}-[disulfide]amylin-MBHA-resin was obtained by treatment of Acm-protected cysteines with thallium (III) trifluoroacetate in trifluoroacetic acid. After cyclization was achieved, the resin and side chain protecting groups were cleaved with liquid HF in the presence of dimethylsulfide and anisole. The ^{29}Pro-h-amylin was purified by preparative HPLC. The peptide was found to be homogeneous by analytical HPLC and capillary electrophoresis and the structure was confirmed by amino acid analysis and sequence analysis. The product gave the desired mass ion. FAB mass spec: $(M+H)^+$=3916.

EXAMPLE H

Preparation of ^{25,28}Pro-h-Amylin

Solid phase synthesis of ^{25,28}Pro-h-amylin using methylbenzhydrylamine anchor-bond resin and N^a-Boc/benzyl-side chain protection was carried out by standard peptide synthesis methods. The ^{2,7}-[disulfide]amylin-MBHA-resin was obtained by treatment of Acm-protected cysteines with thallium (III) trifluoroacetate in trifluoroacetic acid. After cyclization was achieved, the resin and side chain protecting groups were cleaved with liquid HF

in the presence of dimethylsulfide and anisole. The ^{25,28}Pro-h-amylin was purified by preparative reversed-phase HPLC. The peptide was found to be homogeneous by analytical HPLC and capillary electrophoresis and the structure was confirmed by amino acid analysis and sequence analysis. The product gave the desired mass ion. FAB mass spec: $(M+H)^+$=3,939.

EXAMPLE I

Preparation of des-^{1}Lys^{25,28}Pro-h-Amylin

Solid phase synthesis of des-^{1}Lys^{25,28}Pro-h-amylin using methylbenzhydrylamine anchor-bond resin and N^a-Boc/benzyl-side chain protection was carried out by standard peptide synthesis methods. The ^{2,7}-[disulfide]amylin-MBHA-resin was obtained by treatment of Acm-protected cysteines with thallium (III) trifluoroacetate in trifluoroacetic acid. After cyclization was achieved, the resin and side chain protecting groups were cleaved with liquid HF in the presence of dimethylsulfide and anisole. The des-^{1}Lys^{25,28}Pro-h-amylin was purified by preparative reversed-phase HPLC. The peptide was found to be homogeneous by analytical HPLC and capillary electrophoresis and the structure was confirmed by amino acid analysis and sequence analysis. The product gave the desired mass ion. FAB mass spec: $(M+H)^+$=3,811.

EXAMPLE J

Preparation of des-^{1}Lys^{18}Arg^{25,28}Pro-h-Amylin

Solid phase synthesis of des-^{1}Lys^{18}Arg^{25,28}Pro-h-amylin using methylbenzhydrylamine anchor-bond resin and N^a-Boc/benzyl-side chain protection was carried out by standard peptide synthesis methods. The ^{2,7}-[disulfide]amylin-MBHA-resin was obtained

by treatment of Acm-protected cysteines with thallium (III) trifluoroacetate in trifluoroacetic acid. After cyclization was achieved, the resin and side chain protecting groups were cleaved with liquid HF in the presence of dimethylsulfide and anisole. The des-^{1}Lys^{18}Arg^{25,28}Pro-h-amylin was purified by preparative reversed-phase HPLC. The peptide was found to be homogeneous by analytical HPLC and capillary electrophoresis and the structure was confirmed by amino acid analysis and sequence analysis. The product gave the desired mass ion. FAB mass spec: $(M+H)^{+}$=3,832.

EXAMPLE K

Preparation of des-^{1}Lys^{18}Arg^{25,28,29}Pro-h-Amylin

Solid phase synthesis of des-^{1}Lys^{18}Arg^{25,28,29}Pro-h-amylin using methylbenzhydrylamine anchor-bond resin and N^{a}-Boc/benzyl-side chain protection was carried out by standard peptide synthesis methods. The ^{2,7}-[disulfide]amylin-MBHA-resin was obtained by treatment of Acm-protected cysteines with thallium (III) trifluoroacetate in trifluoroacetic acid. After cyclization was achieved, the resin and side chain protecting groups were cleaved with liquid HF in the presence of dimethylsulfide and anisole. The des-^{1}Lys^{18}Arg^{25,28,29}Pro-h-amylin was purified by preparative reversed-phase HPLC. The peptide was found to be homogeneous by analytical HPLC and capillary electrophoresis and the structure was confirmed by amino acid analysis and sequence analysis. The product gave the desired mass ion. FAB mass spec: $(M+H)^{+}$=3,843.

EXAMPLE L

Preparation of des-^{1}Lys^{25,28,29}Pro-h-Amylin

Solid phase synthesis of des-^{1}Lys^{25,28,29}Pro-h-amylin using methylbenzhydrylamine anchor-bond resin and N^{a}-Boc/benzyl-side chain protection was carried out by standard peptide synthesis methods. The ^{2,7}-[disulfide]amylin-MBHA-resin was obtained by treatment of Acm-protected cysteines with thallium (III) trifluoroacetate in trifluoroacetic acid. After cyclization was achieved, the resin and side chain protecting groups were cleaved with liquid HF in the presence of dimethylsulfide and anisole. The des-^{1}Lys^{25,28,29}Pro-h-amylin was purified by preparative reversed-phase HPLC. The peptide was found to be homogeneous by analytical HPLC and capillary electrophoresis and the structure was confirmed by amino acid analysis and sequence analysis. The product gave the desired mass ion. FAB mass spec: $(M+H)^{+}$=3,823.

EXAMPLE M

Preparation of des-^{1}Lys^{25}Pro^{26}Val^{28,29}Pro-h-Amylin

Solid phase synthesis of this h-amylin analogue using methylbenzhydrylamine anchor-bond resin and N^{a}-Boc/benzyl-side chain protection is carried out by standard peptide synthesis methods, and the ^{2,7}-[disulfide]amylin-MBHA-resin obtained by treatment with thallium (III) trifluoroacetate in trifluoroacetic acid. After cyclization is achieved, the resin and side chain protecting groups are cleaved with liquid HF in the presence of dimethylsulfide and anisole. The des-^{1}Lys^{25}Pro^{26}Val^{28,29}Pro-h-amylin is then purified by preparative HPLC.

EXAMPLE N

Preparation of [(D)-^{11}Arg]-Amylin

Solid phase synthesis of this amylin analogue using methylbenzhydrylamine anchor-bond resin and N^{a}-Boc/benzyl-side chain protection is carried out by standard peptide synthesis methods. (D)-^{11}Arg is introduced with Boc-(D)-^{11}Arg(Mtr)-OH. The ^{2,7}-[disulfide]amylin-MBHA-resin, obtained by treatment with thallium (III) trifluoroacetate in trifluoroacetic acid, is cyclized and the resin and side chain protecting groups are cleaved with liquid HF in the presence of dimethylsulfide and anisole. The [(D)-^{11}Arg]-amylin is then purified by preparative HPLC.--

Reworded Paragraphs

Please reword the paragraph bridging pages 19-20 of the originally filed application as follows:

--The receptor binding assay, a competition assay which measures the ability of compounds to bind specifically to membrane-bound amylin receptors, is described in United States Patent No. 5,264,372, issued November 23, 1993, the disclosure of which is incorporated herein by reference. The receptor binding assay is also described in Example 2 below. A preferred source of the membrane preparations used in the assay is the basal forebrain which comprises membranes from the nucleus accumbens and surrounding regions. Compounds being assayed compete for binding to these receptor preparations with ^{125}I Bolton Hunter rat amylin. Competition curves, wherein the amount bound (B) is plotted as a function of the log of the concentration of ligand are analyzed by the computer, using analyses by nonlinear regression to a 4-parameter logistic equation (INPLOT program; GRAPHPAD Software, San Diego, California) or the ALLFIT program of DeLean et al. (ALLFIT, Version 2.7 (NIH, Bethesda, MD 20892)). Munson and Rodbard, Anal. Biochem. 107:220-239 (1980).--

Please reword the paragraph bridging pages 23-24 of the originally filed application as follows:

--Peptides may be purified by RP-HPLC (preparative and analytical) using a Waters DELTA PREP 3000 system. A C4, C8 or C18 preparative column (10 μ, 2.2 X 25 cm; Vydac, Hesperia, CA) may be used to isolate peptides, and purity may be determined using a C4, C8 or C18 analytical column (5 μ, 0.46 X 25 cm; Vydac). Solvents (A=0.1% TFA/water and B=0.1% TFA/CH_3CN) may be delivered to the analytical column at a flowrate of 1.0 ml/min and to the preparative column at 15 ml/min. Amino acid analyses may be performed on the Waters PICO TAG system and processed using the MAXIMA program. Peptides may be hydrolyzed by vapor-phase acid hydrolysis (115°C, 20-24 h). Hydrolysates may be derivatized and analyzed by standard methods (Cohen, et al., The Pico Tag Method: A Manual of Advanced Techniques for Amino Acid Analysis, pp. 11-52, Millipore Corporation, Milford, MA (1989)). Fast atom bombardment analysis may be carried out by M-Scan, Incorporated (West Chester, PA). Mass calibration may be performed using cesium iodide or cesium iodide/glycerol. Plasma desorption ionization analysis using time of flight detection may be carried out on an Applied Biosystems BIO-ION 20 mass spectrometer.--

Please reword the second paragraph on page 27 of the originally filed application as follows:

--If desired, solutions of the above compositions may be thickened with a thickening agent such as methyl cellulose. They may be prepared in emulsified form, either water in oil or oil in water. Any of a wide variety of pharmaceutically acceptable emulsifying agents may be employed including, for example, acacia powder, a non-ionic surfactant (such as a TWEEN), or an ionic surfactant (such as alkali polyether alcohol sulfates or sulfonates, e.g., a TRITON).--

Please reword the first full paragraph on page 34 of the originally filed application as follows:

--To measure ^{125}I-amylin binding, membranes from 4 mg original wet weight of tissue were incubated with ^{125}I-amylin at 12-16 pM in 20 mM HEPES buffer containing 0.5 mg/ml bacitracin, 0.5 mg/ml bovine serum albumin, and 0.2 mM PMSF. Solutions were incubated for 60 minutes at 23°C. Incubations were terminated by filtration through GF/B glass fiber filters (Whatman Inc., Clifton, NJ) which had been presoaked for 4 hours in 0.3% polyethyleneimine in order to reduce nonspecific binding of radiolabeled peptides. Filters were washed immediately before filtration with 5 ml cold PBS, and immediately after filtration with 15 ml cold PBS. Filters were removed and radioactivity assessed in a gamma-counter at a counting efficiency of 77%. Competition curves were generated by measuring binding in the presence of 10^{-12} to 10^{-6} M unlabeled test compound and were analyzed by nonlinear regression using a 4-parameter logistic equation (INPLOT program; GRAPHPAD Software, San Diego).--

Please reword the paragraph bridging pages 35-36 of the originally filed application as follows:

--Muscles were added to 50mL Erlenmeyer flasks containing 10mL of a pregassed Krebs-Ringer bicarbonate buffer containing (each liter) NaCl 118.5 mmol (6.93g), KCl 5.94 mmol (443mg), $CaCl_2$ 2.54 mmol (282mg), $MgSO_4$ 1.19 mmol (143mg), KH_2PO_4 1.19 mmol (162mg), $NAHCO_3$ 25 mmol (2.1g), 5.5mmol glucose (1g) and recombinant human insulin (HUMILIN-R, Eli Lilly, IN) and the test compound, as detailed below. pH at 37° was verified as being between 7.1 and 7.4. Muscles were assigned to different flasks so that the 4 muscle pieces from each animal were evenly distributed among the different assay conditions. The incubation media were gassed by gently blowing carbogen (95% O_2, 5% CO_2) over the surface while being continuously agitated at 37°C in an oscillating water bath. After a half-hour "preincubation" period, 0.5μCi of U-^{14}C-glucose was added to each flask which was incubated for a further 60 minutes. Each muscle piece was then rapidly removed, blotted and frozen in liquid N_2, weighed and stored for subsequent determination of ^{14}C-glycogen.—

Please reword the paragraph bridging pages 38-39 of the originally filed application as follows:

--Gastric emptying was measured using a modification (Plourde et al., Life Sci. 53:857-862 (1993)) of the original method of Scarpignato et al. (Arch. Int. Pharmacodyn. Ther. 246:286-295 (1980)). Briefly, conscious rats received by gavage 1.5 mL of an acoloric gel containing 1.5% methyl cellulose (M-0262, Sigma Chemical Co., St. Louis, MO) and 0.05% phenol red indicator. Twenty minutes after gavage, rats were anesthetized using 5% halothane, the stomach exposed and clamped at the pyloric and lower esophageal sphincters using artery forceps, removed and opened into an alkaline solution which was made up to a fixed volume. Stomach content was derived from the intensity of the phenol red in the alkaline solution, measured by absorbance at a wavelength of 560 nm. In most experiments, the stomach was clear. In other experiments, particulate gastric contents were centrifuged

to clear the solution for absorbance measurements. Where the diluted gastric contents remained turbid, the spectroscopic absorbance due to phenol red was derived as the difference between that present in alkaline vs acetified diluent. In separate experiments on 7 rats, the stomach and small intestine were both excised and opened into an alkaline solution. The quantity of phenol red that could be recovered from the upper gastrointestinal tract within 29 minutes of gavage was 89 ± 4%; dye which appeared to bind irrecoverably to the gut luminal surface may have accounted for the balance. To compensate for this small loss, percent of stomach contents remaining after 20 minutes were expressed as a fraction of the gastric contents recovered from control rats sacrificed immediately after gavage in the same experiment. Percent gastric emptying contents remaining = (absorbance at 20 min)/(absorbance at 0 min). Dose response curves for gastric emptying were fitted to a 4-parameter logistic model using a least-squares iterative routine (ALLFIT, v2.7, NIH, Bethesda, MD) to derive ED_{50}s. Since ED_{50} is log-normally distributed, it is expressed ± standard error of the logarithm. Pairwise comparisons were performed using one-way analysis of variance and the STUDENT-NEWMAN-KEULS multiple comparisons test (INSTAT v2.0, GRAPHPAD Software, San Diego, CA) using $P < 0.05$ as the level of significance.—

Please add the following new claims 7-16:

7. (New) A method of treating obesity in a human subject comprising administering to said subject an amount of a composition comprising an amylin or an amylin agonist effective to treat obesity, with the proviso that the composition does not contain a cholecystokinin or a cholecystokinin agonist.

✓ 8. (New) The method of claim 1, 2 or 3 wherein said treatment of obesity of said subject comprises administration of said effective amount of an anti-obesity agent consisting of an amylin or an amylin agonist for at least about four weeks.